REMARKS

The pending claims are claims 1-21, 31-38, 40-48, 53-58, and 60-64.

Amendment to the Claims

Claims 1, 3, 12, 31, 32, 42, 53, 56, and 63 have been amended. Claim 59 has been cancelled without prejudice. New claims 54-67 have been added.

No new matter has been added herein.

Claim Objections

In the June 1, 2007 Office Action, claim 63 was objected to for the misspelling of the word "hardness." The inadvertent error was corrected thereby obviating this objection.

In addition, claim 53 was objected to because the phrase "combining excipients to said second solution" was considered grammatically awkward. Consistent with the Examiner's suggestions, applicants have substituted the word "with" for "to," thereby obviating this objection.

Claim Rejections – 35 U.S.C. §112, Written Description Requirement

In the June 1, 2007 Office Action, claims 1-21, 31-38, 40-48, 53-56 and 58-59 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for containing subject matter that was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each specific rejection is discussed below.

1. The Examiner indicated that applicants failed to provide adequate written support for the limitation in claims 1, 31 and 53 of dissolving the salt or free base of the active pharmaceutical

ingredients (API) in a first solvent to form a first solution at any other conditions other than those that do not cause decomposition of the active pharmaceutical ingredients. In response, applicants have amended claims 1, 31 and 53 to recite that the "active pharmaceutical ingredients are dissolved under conditions that will not cause decomposition of said active pharmaceutical ingredients, including pH in a range form about 3 to about 11" thereby obviating this rejection. Support for this amendment can be found in the instant specification in part at page 9, lines 9-10. Withdrawal of the rejection of claims 1, 31 and 53, and claims depending therefrom, is respectfully requested.

2. The Examiner indicated that applicants failed to provide adequate written support for the limitation in claim 53 that the compositions have reduced variability in API and increased certainty that said API are delivered within a therapeutic range. Applicants traverse such rejection.

It is well established that to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003). In addition to the disclosure referred to by the Examiner (page 4, lines 6-10), applicants also recited:

> "However, the purity of the commercially available tannate compounds is variable. The stoichiometry of the free base to tannic acid in the raw material is different from batch to batch. This causes significant dosing and processing problems during manufacture.
>
> Therefore, in the present manufacturing process, commonly available salts of the API are converted in-situ into the tannate salt and subsequently incorporated into the tablet." (see, instant specification, page 15, lines 8-14)

Considered together, one skilled in the art could reasonably conclude that applicants had possession of "a composition consisting of pyrilamine tannate, phenylephrine tannate and dextromethorphan tannate with reduced variability in active pharmaceutical ingredient content and increased certainty that said active pharmaceutical ingredients are delivered within a therapeutic range."

That said, the offending claim language was excised to advance prosecution of the presently

pending claims. Withdrawal of the rejection of claim 53 is respectfully requested.

3. The Examiner indicated that applicants failed to provide adequate written support for the limitation in claim 59 that the compositions have reduced variability in API and increased certainty that said API are delivered within a therapeutic range. Applicants traverse such rejection.

Similar to claim 53, applicants disagree with the Examiner, however, to advance prosecution of the presently pending claims, claim 59 has been cancelled herein.

Withdrawal of the rejection of claims 1-21, 31-38, 40-48, 53-56 and 58-59 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

In the June 1, 2007 Office Action, claims 1-21, 31-38, 40-48, and 53-39 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse said rejection.

Each specific rejection is discussed below.

1. The Examiner objected to the phrase "without isolation or purification," and stated:

> "[i]t is noted that the claims as presently written still do not clearly set forth that it is the *tannate salts* that are not isolated or purified prior to their combination with the liquid pharmaceutical carrier, powder mixture or dispersion." (see, e.g., Office Action dated June 1, 2007, at page 7, lines 5-7) (emphasis in original)

Applicants have amended claims 1, 31, and 53 to excise the "without isolation or purification" language and include "wherein the tannate salts of the active pharmaceutical ingredients are not purified nor dried subsequent to formation." Support for this amendment can be found throughout the specification, e.g., page 6, lines 1-4.

Accordingly, applicants respectfully request that the Examiner withdraw the rejection of claims

1-21, 31-38, 40-48, and 53-39 under 35 U.S.C. §112, second paragraph.

2. The Examiner indicated that claims 3 and 32 fail to clearly delineate how the "free base" form of the API is in the form of a maleate, citrate, chloride, bromide, acetate or sulfate salt. In response, applicants have excised the "free base" limitation from claims 1, 3, 31, 32, 53 and 56, thereby obviating this rejection. Withdrawal of same is respectfully requested.

3. The Examiner indicated that claims 12 and 42 recite a trademark (i.e., MAGNASWEET MM-100), which renders the scope of the claims indefinite. In response, applicants have excised the term Magnasweet MM-100 from claims 12 and 42, thereby obviating this rejection. Withdrawal of same is respectfully requested.

4. The Examiner indicated that claim 53 was indefinite because it was unclear whether the limitation of "tannate salts" at line 3 of the claim was intended to solely modify the dextromorphan component or whether it was intended to modify the phenylephrine and pyrilamine components as well. In response, applicants have included "tannate" after the phenylephrine and pyrilamine recitations, thereby obviating this rejection. Withdrawal of same is respectfully requested.

Withdrawal of the rejection of claims 1-21, 31-38, 40-48, and 53-39 under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claim Rejections Under 35 U.S.C. §103(a)

In the June 1, 2007 Office Action, claims 1-21, 31-38, 40-48 and 53-64 were rejected under 35 U.S.C. §103(a) as being unpatentable over Gordziel (U.S. Patent No. 6,287,597, hereinafter "Gordziel") in view of Venkataraman (U.S. Patent No. 6,509,492, hereinafter "Venkataraman") and Chopdekar *et al.* (U.S. Patent No. 5,599,846, hereinafter "Chopdekar"), further in view of Singh et al. (U.S. Patent No. 5,759,579) (hereinafter Singh). Specifically, the Examiner stated that:

> "One of ordinary skill in the art would have found it *prima facie* obvious to combine disclosures of Gordziel and Venkataraman to compose a pharmaceutical composition of phenylephrine tannate, pyrilamine tannate and dextromethorphan tannate because Venkataraman teaches the preferable combination of an

antihistamine, decongestant and antitussive (i.e., dextromethorphan tannate, see Table 1 at col. 7) as an efficacious and comprehensive approach to treating viral infection or symptoms, cold symptoms, allergic rhinitis, runny nose, cough, post-nasal drip, rhinorrhea and sinusitis (Venkataraman, col. 8, lines 5-27). The skilled artisan would have been motivated to do so in order to provide a single composition with broader therapeutic effects and an enhanced benefit to the patient. Additionally, both the compositions of Gordziel and those of Venkataraman are each known for the same therapeutic purpose (i.e., treating the common cold, allergic rhinitis, sinusitis, etc.) and, therefore, the combination of the composition of Gordziel with that of Venkataraman would have naturally commended itself, and have been *prima facie* obvious, to the skilled artisan. Motivation to administer two compositions flows logically from the fact that each was known to be administered for the same therapeutic endpoint and it is generally obvious to use in combination two or more agents that have previously been used separately for the same purpose. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069.

Additionally, it is noted that it would have been prima facia obvious to one of ordinary skill in the art at the time of the invention to employ the process of Chopdekar et al. for formulation of the tannate salts of phenylephrine, pyrilamine and dextromethorphan rather than the conventional isopropanol route because the process of Chopdekar et al. is capable of producing (a) a much higher yield of tannate(s) and (b) a much higher level or purity of those tannate(s), as compared with the synthetic isopropanol route. Such a person would have been motivated to do so because the enhanced yield and purity would have allowed for greater uniformity in the pharmaceutical composition and would also have enhanced the therapeutic effect of the composition while minimizing exposure to degradation products and organic solvents, which may hinder the therapeutic activity of the composition.

Though the process of Chopdekar et al. is not necessarily the same as that presently recited in the claims in the order or step by which the process proceeds, the invention as claimed is the composition of phenylephrine tannate, pyrilamine tannate, and dextromethorphan tannate, regardless of how Applicant has claimed the composition is produced. Process limitations only become patentable distinctions if they confer upon the product a physical or structural property that is not found in the composition of the prior art (see, e.g., Office Action dated October 30, 2006, at page 13, line 24 through page 15, line 5).

Applicants respectfully traverse this rejection.

The present invention generally provides for a pharmaceutical composition ***consisting of*** tannate salts of phenylephrine, pyrilamine and dextromethorphan together with a dispersing agent and either a liquid or granulate pharmaceutical carrier.

Gordziel describes a composition consisting essentially of pyrilamine tannate and phenylephrine tannate (see, e.g., Gordziel at Abstract). Importantly, Gordziel only discusses the combination of two sympathomimetic drugs – pyrilamine and phenylephrine - not the combination of sympathomimetic drugs and other non-sympathomimetic drugs such as antitussives, expectorants, etc.

The addition of Venkataraman does not remedy the deficiency of the Gordziel reference. According to the Examiner, "Venkataraman teaches the preferable combination of an antihistamine, decongestant and antitussive." In actuality, Venkataraman recites that the preferred tannate compositions may comprise a single agent (e.g., antihistamine, decongestant, antitussive, or expectorant) or may comprise two or more pharmaceutical classes including:

> "an antihistamine and a decongestant; an antihistamine and an antitussive; an antihistamine and an expectorant; and antihistamine, a decongestant and an antitussive; and antihistamine, a decongestant, an antitussive and an expectorant; an antihistamine, an antitussive and an expectorant; a decongestant and an antitussive; a decongestant and an expectorant; a decongestant, an antitussive and an expectorant; an antitussive and an expectorant." (see, Venkataraman, col. 10, lines 4-13)

It is unclear how the Examiner knew that the preferable combination in Venkataraman is an antihistamine, a decongestant and an antitussive when Venkataraman discloses at least ten different combinations including two or more pharmaceutical classes. In other words, one skilled in the art considering Venkataraman would be just as likely to select a composition consisting of an antihistamine and an expectorant as they would to select a composition consisting of an antihistamine, a decongestant and an antitussive. In short, one skilled in the art considering Gordziel's teaching had at least a 90% chance of being distracted by the Venkataraman teaching whereby a completely different combination of ingredients may be considered – after all Venkataraman, like Gordziel, claims to treat upper respiratory conditions. Even assuming that one skilled in the art selected a composition consisting of an antihistamine, a decongestant and an antitussive, Venkataraman actually discloses that the favored antihistamines are

chlorpheniramine, brompheniramine and diphenhydramine (see, Venkataraman, col. 7, lines 43-57). Accordingly, the likelihood that one skilled in the art would combine Gordziel and Venkataraman and come up with applicants' claimed composition consisting of the active ingredients phenylephrine, pyrilamine and dextromethorphan (and not change the antihistamine in the process) is not as reasonable as the Examiner contends.

The foregoing compels the conclusion that the rejection is based solely on hindsight, which is impermissible. The courts have made it clear that Examiner's must not use the applicants' own disclosure as a blueprint to arbitrarily piece together isolated features described in the references (where no teaching or suggestion to combine the references is present) in an attempt to re-create applicants' claimed invention. Merely identifying all of the elements of a claim or their equivalents in the prior art is not sufficient. Almost all inventions are combination of old elements, and an Examiner may often find every element of a claimed invention in the prior art. If this finding were sufficient "to negate patentability, very few patents would ever issue." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Therefore, in order to establish a *prima facie* rejection for obviousness, an "examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would [***not*** could] select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

The addition of the Chopdekar reference does not remedy the deficiencies of the Venkataraman and Gordziel references. Chopdekar describes a process for the preparation of phenylephrine tannate only. Specifically, phenylephrine free *base* is dissolved in water and contacted with tannic acid to form a reaction mixture including insoluble phenylephrine tannate. The water is removed by subjecting the entire reaction mixture to freeze-drying to yield solid phenylephrine tannate. Notably, in the event that the phenylephrine reactant is in the form of a **salt**, e.g., as phenylephrine HCl, Chopdekar teaches the dissolution of the phenylephrine **salt** in cold water and neutralization with NaOH or KOH, whereby the phenylephrine free *base* precipitates out and can be recovered by filtration, rinsed and air dried at ambient temperatures for subsequent contact with tannic acid (see, Chopdekar, col. 2, lines 41-52).

Importantly, referring to claim 1, applicants' phenylephrine reactant is in the form of a **salt** and the conditions that will not cause decomposition of said active pharmaceutical ingredients include pH in a range from about 3 to about 11. It is well understood by those skilled in the art that a pH

of 11 corresponds to a concentration of OH^- of 1×10^{-3} M. Clearly, a composition having $[OH^-] = 1 \times 10^{-3}$ M would not serve as an effective neutralizing solution, as required by Chopdekar.[2] Moreover, Chopdekar requires that the phenylephrine free *base* formed subsequent to neutralization be rinsed thoroughly (to remove the **salt**, e.g., chloride) and dried prior to resolubilization in water and contact with tannic acid. The reactions are not the same and one cannot reasonably expect that the products will be the same.

In short, Chopdekar reports a high yield of tannates when the reactant is a phenylephrine free *base*, not phenylephrine **salt**. Unexpectedly, applicants were able to achieve very high yield rates using salts of the active pharmaceutical ingredients.

Furthermore, Chopdekar describes a process for the preparation of phenylephrine tannate only. There is no disclosure relating to the inclusion of a dispersing agent in the Chopdekar reaction mixture to prevent clumping and aggregation of the tannate salt formed. Accordingly, one cannot reasonably expect that the adaptation of the Chopdekar reference to include the simultaneous formation of the phenylephrine, pyrilamine and dextromethorphan tannate salts would result in the formation of high purity tannate salts. Couple this with the fact that Chopdekar discloses the use of a free *base* reactant instead of a **salt** reactant and one can easily conclude that the products formed using the method of Chopdekar are different than applicants' claimed products.

Singh does not cure the deficiencies of Gordziel, Venkataraman and Chopdekar. Singh relates to the pharmaceutically acceptable liquid excipient suspending base for homogeneously suspending solid pharmaceutically active compounds. In other words, Singh relates to the suspension of already formed solid pharmaceutical salts, most of which are disclosed as maleates, HCl, or HBr, in an excipient without excessive foam formation. There is absolutely no disclosure in Singh relating to the specific combination of phenylephrine, pyrilamine and dextromethorphan, much less a high purity composition whereby the tannate salts of phenylephrine, pyrilamine and dextromethorphan are produced in situ.

In summary, upon combination of Gordziel, Venkataraman, Chopdekar, and Singh, as suggested by the Examiner, there is no reasonable expectation that applicants' claimed composition may be successfully produced. Accordingly, applicants submit that the claimed invention is patentable over the cited references, taken alone or in combination, and respectfully request reconsideration

[2] Otherwise weak bases, e.g., NH_3, would have been disclosed for neutralization purposes.

and withdrawal of the rejection.

Obviousness-Type Double Patenting

In the June 1, 2007 Office Action, the Examiner provisionally rejected claims 1-21, 31-38, 40-48 and 53-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 and 31-48 of co-pending U.S. Patent Application No. 10/047,578.

When the obviousness-type double patenting rejection is the only rejection remaining to the presently pending case AND **if** the presently pending claims are an obvious variation of the invention defined in claims 1-21 and 31-48 of co-pending U.S. Patent Application No. 10/047,578 (which can only be objectively assessed when the only rejection remaining in the presently pending case is the obviousness-type double patenting rejection), Applicants will consider submitting the required terminal disclaimer.

Petition for Extension of Time/Fees Payable

Applicants hereby petition for a two (2) month extension of time, extending the deadline for responding to the June 1, 2007 Office Action from September 1, 2007 to November 1, 2007. The fee of $225.00 specified in 37 C.F.R. §1.17(a)(2) for such two (2) month extension is hereby enclosed.

The total fee of $225.00 is being paid by Electronic Funds Transfer. Authorization is hereby given to charge any deficiency in applicable fees for this response to Deposit Account No. 13-4365 in the name of Moore & Van Allen, PLLC.

Conclusion

Claims 1-21, 31-38, 40-48, 53-58 and 60-64 are in form and condition for allowance. If any additional issues remain, the Examiner is requested to contact the undersigned attorney at (919) 286-8090 to discuss same.

Respectfully submitted,

MOORE & VAN ALLEN PLLC

Date: Oct. 2, 2007

By: _____

Tristan A. Fuierer
Registration No. 52,926
Moore & Van Allen PLLC
430 Davis Drive, Suite 500
Morrisville, NC 27560-6832
Telephone: (919) 286-8000
Facsimile: (919) 286-8199